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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,174	REED ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-28,42-45,76,77 and 142-163* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-28,42-45,76,77 and 142-163* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 3/21/2005. The amendment has been entered. Claims 2, 3, 29-41, 46-75 and 78-141 have been cancelled. New claims 142-163 have been added. Claims 1, 4-28, 42-45, 76, 77 and 142-163 are currently pending in the application and are examined herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Specification

The amendment filed 3/21/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the specific nucleic acid sequence of EST Accession No. AA098865 (i.e., SEQ ID NO: 37) (e.g., see the amendment to page 3 and 13 of the specification).

The USPTO recommends full disclosure of each sequence in full compliance with rules 37 CFR 1.821-1.825. However, a copending U.S. patent application, prior art document or database accession number that discloses sequence(s) may be incorporated by reference in compliance with 37 CFR 1.57.

MPEP section 608.01 requires that the incorporation by reference be expressly presented in the specification to be effective.

If there was an express incorporation by reference of the uniquely identified source document in accordance with 37 CFR 1.57(b), then an amendment accompanied by a statement in accordance with 37 CFR 1.57(f) would not be considered new matter. A claim that identifies a sequence by database accession number will usually be accepted as clear intent to incorporate the sequence by reference. This claim must be an original claim that is present as of the filing date. It is noted that 37 CFR 1.57 (f) states:

> "Any insertion of material incorporated by reference into the specification or drawings of an application must be by way of an amendment to the specification or drawings. Such an amendment must be accompanied by a statement that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter." (Emphasis Added)

In the instant case, the Accession number was recited in the original claims, indicating a clear intent to incorporate the sequence by reference. However, Applicants have not submitted a statement in accordance with 37 CFR 1.57(f). Therefore, the amendment is considered new matter.

Applicant is required to either cancel the new matter or to make a proper incorporation by reference as indicated in MPEP section 608.01(p) (and new rule 37 CFR 1.57, especially in the reply to this Office Action.

Claim Objections

Claims 24-28 are objected to for encompassing non-elected subject matter. The claims encompass two patently distinct Inventions for the reasons of record. Specifically, the claims

encompass a polynucleotide sequence that encodes a polypeptide that inhibits apoptosis or an antisense molecule that stimulates or induces apoptosis. Applicants elected the group drawn to a polynucleotide sequence that encodes a polypeptide that inhibits apoptosis. However, the claims still read on the non-elected invention. The non-elected Invention has been withdrawn from consideration for the reasons set forth in the previous Office Action. The instant claims are examined to the extent that they read n the elected Invention.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-28, 42-45, 142-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 15 are drawn to an isolated polynucleotide sequence wherein the sequence is distinct from EST Accession number AA098865, which is... SEQ ID NO: 37. The phrase "which is ...(SEQ ID NO: 37)" renders the claim indefinite because it is unclear if "which refers to the isolated polynucleotide or to the Accession number. Therefore, it is unclear if the isolated polynucleotide sequence is SEQ ID NO: 37 or if the isolated polynucleotide is distinct from SEQ ID NO: 37. Claims 2-14 and 16-28 are dependent claims which are rejected for the same reasons because they encompass all of the limitations of the independent claim(s).

Claim 42 is drawn to An isolated nucleic acid having at least 70% identity to SEQ ID NO: 1, which is SEQ ID NO: 37), wherein the nucleic acid encodes a polypeptide that modulates apoptosis. The phrase "the nucleic acid" in line 5 of the claim renders the claim indefinite because it is unclear if "the nucleic acid" refers to SEQ ID NO: 1 or SEQ ID NO: 37. Claims 43-45 are dependent claims which are rejected for the same reasons because they encompass all of the limitations of claim 42. As such, the claim can be interpreted being drawn to the nucleic acid that is SEQ ID NO: 37 wherein SEQ ID NO: 37 encodes a polypeptide that modulates apoptosis.

Claim 142 is drawn to: "An isolated or recombinant nucleic acid comprising a polynucleotide sequence SEQ ID NO: 1, wherein the sequence is distinct from EST Accession no. AA098865, which is... (SEQ ID NO: 37)". The phrase "nucleic acid comprising a polynucleotide sequence SEQ ID NO: 1" renders the claim indefinite because it is unclear if the nucleic acid comprises a polynucleotide sequence that is SEQ ID NO: 1 or a polynucleotide of SQE ID NO: 1. Therefore, the phrase "an isolated or recombinant nucleic acid comprising a polynucleotide sequence SEQ ID NO: 1, wherein the sequence is distinct from: (SEQ ID NO: 37)" renders the claim indefinite in view of the limitations "distinct from SEQ ID NO: 37" and "wherein the sequence is from 15 base pairs to 2.5kB in length" (e.g., see claim 148). It is noted tat SEQ ID NO: 1 is 887 nucleotides long therefore it is unclear how the sequence could be 15 base pairs unless the claim encompassed sequences of SEQ ID NO: 1. Claims 143-163 are dependent claims which are rejected for the same reasons because they encompass all of the limitations of claim 142.

In the interest of compact prosecution, claim 142 is interpreted as "An isolated or recombinant nucleic acid comprising a polynucleotide sequence of SEQ ID NO: 1, wherein the sequence is distinct SEQ ID NO: 37".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-28, 42-45, and 142-163 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure

of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure. (Emphasis added).

In the instant case, the claims encompass the new limitations: "polynucleotide having greater than 91.6% identity to SEQ ID NO: 1", SEQ ID NO: 37 (i.e., the specific nucleic acid sequence of EST Accession No. AA098865) (e.g., see claims 1, 15, 17, 42, 142), and isolated or recombinant nucleic acid... which is (SEQ ID NO: 37), which encodes a polypeptide that modulates apoptosis", are considered new matter (e.g., see claim 1, 15, 17, 42, 142) because the original specification does not explicitly disclose the indicated limitations. See MPEP § 2163.06.

It is noted that *Lockwood v. American Airlines Inc.,* 41 USPQ2d 1961, 1966 (CAFC 1997) indicates: "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose."

It is apparent that the applicants at the time the invention was made did not intend or explicitly contemplate using a sequence "greater than 91.6% identity to SEQ ID NO: 1" as part of their invention. There is no evidence in the specification that the applicants were in possession of sequences "greater than 91.6% identity to SEQ ID NO: 1", other than SEQ ID NO: 1 itself, at the time of invention. Furthermore, it is apparent that the applicants at the time the invention was made did not intend or explicitly contemplate SEQ ID NO: 37 encoded a

polypeptide that modulates apoptosis as part of their invention (e.g., see claim 42). Nor is there evidence in the specification that the applicants identified SEQ ID NO: 37 as a nucleic acid encoding a polypeptide that modulates apoptosis, at the time of invention.

With respect to the newly added sequence of SEQ ID NO: 37, it is noted that the Accession number was recited in the original claims, indicating a clear intent to incorporate the sequence by reference (as indicated above). However, Applicants have not submitted a statement in accordance with 37 CFR 1.57(f). Therefore, the amendment is considered new matter.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, the instant claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-10, 12-23, 26-28, 42-45, 76 and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

The instant claims are drawn to an isolated/recombinant nucleic acid that has a specified level of identity to SEQ ID NO:1 (e.g., sequences having greater than 91.6% identical, see claims 1, 17) as well as a nucleic acid sequence encoding a polypeptide that is at least 65% identical to SEQ ID NO: 2 (e.g., see claim 76). It is noted that sequences having greater than 91.6% identity to SEQ ID NO: 1 includes any sequences which have within them a segment of sequence that is greater than 91.6% identical to any part of SEQ ID NO: 1. As such, the claims are drawn to a genus of nucleic acid sequences which are different from the sequences explicitly disclosed in the specification. The genus of claimed nucleic acid sequences encompass an indefinite number of distinct nucleic acid sequences (possibly millions) considering every possible nucleic acid sequence that is encompassed by the claims including sequences which have yet to be identified. It is noted that for claims 1, 4-10, 12-23, 26-28, 76 and 77, the claims do not specifically indicate any particular function for the nucleic acids encompassed by the claims. As such claims 1-10, 12-23, 26-28, 76 and 77 encompass nucleic acid molecules that could have completely unrelated

functions or which are non-functional, yet still meet the sequence identity limitations of the claims. Furthermore, regarding "modulating apoptosis" the specification does not disclose any structure-function relationship for the claimed genus of sequences that would identify the elements of the sequences that are critical for their function. As such, the specification has not disclosed which sequences that meet the limitations set forth in the claims (other than SEQ ID NO:1 itself) would have the desired function (i.e., modulating apoptosis) and which sequences encompassed by the claims would not have the desired function. Therefore, the specification has failed to adequately describe the genus of sequences encompassed by the claims.

It is noted that amending the claims to the nucleic acid that is SEQ ID NO:1 or a nucleic acid sequence encoding SEQ ID NO: 2 would obviate this rejection.

Additionally, claims 1, 4-10, 12-23, 26-28, 42-45, 76 and 77 are also rejected under 35 U.S.C. 112, first paragraph (in view of the written description rejection above), because the specification, while being enabling for the indicated claims wherein the claims are limited to SEQ ID NO:1 or a nucleic acid encoding SEQ ID NO: 2, does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As mentioned above, the claims encompass sequence for which there is insufficient written description provided in the specification. Without a clear disclosure of the sequences encompassed by the claims one of skill in the art would not know how to make or use the

claimed invention without performing an undue amount of additional experimentation to first identify the sequences having the desired function.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-28, 76, 77, 142-163 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/00506 (KATO et al.).

Claim 1 (and its dependent claims) are drawn to an isolated or recombinant nucleic acid comprising a polynucleotide sequence having greater than 91.6% identity to SEQ ID NO: 1 wherein the sequence is distinct from SEQ ID NO: 37. The phrase "a polynucleotide sequence having greater than 91.6% identity to SEQ ID NO: 1" is interpreted as encompassing a polynucleotide sequence wherein any portion of the sequence is greater than 91.6% identical to any part of SEQ ID NO: 1, which is consistent with the isolated nucleic acid being distinct from SEQ ID NO: 37.

Claim 142 (and its dependent claims) is drawn to an isolated or recombinant nucleic acid comprising a polynucleotide sequence SEQ ID NO: 1, wherein the sequence is distinct from EST Accession no. AA098865, which is... (SEQ ID NO: 37)". As indicated above it is unclear if the nucleic acid comprises a polynucleotide sequence that is SEQ ID NO: 1 or a polynucleotide of SEQ ID NO: 1. As such, claim 142 is interpreted as "An isolated or recombinant nucleic acid

comprising a polynucleotide sequence of SEQ ID NO: 1, wherein the sequence is distinct SEQ ID NO: 37", which appears to be consistent with claim 148 which indicates that the nucleic acid is 15 base pairs to 2.5kB in length.

KATO teaches an isolated nucleic acid sequence (see SEQ ID NO:23 of KATO) wherein SEQ ID NO: 23 of KATO comprises a sequence that is 100% identical to SEQ ID NO: 1. Specifically, Nucleotides 1-700 are 100% identical to nucleotides 74-774 of SEQ ID NO: 1 (e.g., see sequence alignment of previous Office Action). SEQ ID NO:23 of KATO is a sequence that is 1168 nucleotides in length (e.g., see Sequence Listing page 20/45). Furthermore, KATO teaches cDNA fragments (more than 10 bp) including antisense nucleotide sequences that can be used as probes (e.g., see p. 11, lines 8-15) that hybridize to related DNA sequences (e.g., see p. 12, lines 5-8). It is noted that the specification does not disclose a limiting definition of "stringent hybridization conditions", therefore any conditions can be considered stringent conditions. In view of the open definition of "stringent hybridization conditions" SEQ ID NO: 23 of KATO as well as the probes described by KATO would necessarily hybridize to SEQ ID NO:1. Furthermore, the probes described by KATO (e.g., p.11-12) would also encompass probes that are subsequences of SEQ ID NO:1 that are at least 15bp long. KATO also teaches that the probes can be attached to a "gene chip" or other support (e.g., see p. 12 lines 10-15). It is noted that the specification does not appear to explicitly define the limitation "substrate"; therefore, given the broadest reasonable interpretation consistent with the specification, the attachment of the nucleic acid to a "gene chip" (as taught by KATO, e.g. page 12) would constitute attaching the sequence to a substrate. Furthermore, hybridizing a sequence to the nucleic acid sequence (e.g., such as a examining expression patterns—see p. 12) would

constitute attaching a plurality of sequences (i.e., a plurality of nucleotides) to a substrate at defined positions. KATO also teaches that the nucleic acid sequence that meets the instant limitations can be comprised in an expression vector such that the vector operably encodes and expresses the polypeptide encoded therein (e.g., see p. 7 lines 2-23). KATO teaches that the expression construct can have a promoter, such as the cytomeglovirus (CMV) promoter (a constitutive promoter) wherein the construct can express the encoded polypeptide in a cell, including a mammalian cell. KATO also teaches the construct can be comprised in a viral vector such as an EBV vector (it is noted that EBV is a herpes virus) (e.g., see p. 7). Furthermore, KATO teaches that the vector can be transformed into cell wherein the cell is a bacterial cell or a eukaryotic cell, including a mammalian cell (e.g., see p. 7, lines 2-23).

Therefore, KATO anticipates the instant claims.

Response to Arguments

With respect to the indication that claims 24, 25, and 29-141 were withdrawn from consideration, it is noted that only the non-elected subject matter was withdrawn from consideration for the reasons indicated herein. Claims 29-41, 46-75 and 78-141, were properly withdrawn from consideration for the reasons of record. The Examiner apologizes for any confusion. The claims have been considered to the extent that they read on the elected subject matter and the non-elected subject matter has been withdrawn from further consideration for the reasons of record.

Applicant's arguments filed 3/21/2005 have been fully considered and are addressed below.

With respect to the amendment adding the sequence of SEQ ID NO: 37, it is noted that the inclusion of the Accession No. in the original claim indicating a clear intent to incorporate the sequence by reference. However, Applicants have not submitted a statement in accordance with 37 CFR 1.57(f). Therefore, the amendment is considered new matter. Submitting a statement in accordance with 37 CFR 1.57(f) is required in order to overcome the new matter rejection.

It is noted that 37 CFR 1.57 (f) states:

> "Any insertion of material incorporated by reference into the specification or drawings of an application must be by way of an amendment to the specification or drawings. Such an amendment must be accompanied by a statement that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter." (Emphasis Added)

With respect to the rejection of claims under 35 USC 112, 2nd paragraph, the amendment has overcome the rejection. However, the amendment has necessitated new rejection(s) under 35 USC 112, 2nd paragraph for the reasons indicated herein.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (written description), Applicants argue that the percentage of identity recited in the claims provide sufficient relevant identifying characteristics to meet the standard (see p19 of the response filed 3/21/2005). Applicants also refer to the Guidelines for Examination which state that the policy goals are to (i) clearly convey to the public what was invented, (ii) put the public in possession of what the applicant claims as the invention; and (iii) prevent an applicant from claiming subject matter that was not described in the specification as filed. Applicants also assert that possession

of the claimed invention can be shown by any of: (1) actual reduction to practice, (2) a clear depiction of the invention in detailed drawings; or (3) a description of sufficient relevant identifying characteristics. Applicants contend that these requirements are met because there is actual reduction to practice in terms of the recitation of SEQ ID NO:1 and the protein encoded by this sequence, SEQ ID NO:2.

In response, the policy goals indicated by the Guidelines are acknowledged. It is agreed that the policy goals are as stated and that the possession can be shown as indicated. However, in the instant case, the specification does not provide sufficient description of the claimed sequences. In order to determine if a sufficient description has been provided, the breadth of the genus of sequences encompassed by the claims must be considered. In the instant case, the claims encompass any nucleic acid sequence that is greater than 91.6% identical to SEQ ID NO: 1. It is noted that the broad claims do not indicate any particular function for the sequences. As such, the claims encompass sequences which have completely different function as well as sequences which are non-functional. It is not apparent from the disclosure that Applicants have identified any particular structural elements of the sequences such as any conserved functional domains such that one of skill in the art would know which variants retained the same function as a nucleic acid encoding SEQ ID NO: 2. Since one of skill in the art would not be able to identify which variants of SEQ ID NO: 1 would be functional variants without performing additional experimentation, the specification has not provided a sufficient description. Thus, the specification has not clearly convey to the public what was invented or put the public in possession of what the applicant claims as the invention.

With respect to Applicants' assertion that the description requirements are met because there is actual reduction to practice in terms of the recitation of SEQ ID NO:1 and the protein encoded by this sequence, SEQ ID NO:2, it is respectfully pointed out that the claim are not limited to a nucleic acid encoding SEQ ID NO: 2. Rather the claims encompass nucleic acid sequences which encode variants of SEQ ID NO: 2 wherein it is not clear what function, if any, the variants would be. It is acknowledged that the specification has disclosed an adequate description to support a genus limited to any nucleic acid that encodes SEQ ID NO: 2, and limiting the claims a such would over come the instant rejection.

Furthermore, *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Additionally, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only isolated nucleic acids encoding the amino acid sequence set forth in SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

With respect to Applicants arguments concerning the phrase "modulating apoptosis" it is acknowledged that proteins capable of "modulating apoptosis" based on their binding partners is known in the art. The instant rejection does not question if proteins capable of "modulating apoptosis" are possible. Rather the instant rejection is merely in view of the fact that the specification has not disclosed the structural elements of sequences encompassed by the claims such that one of skill in the art would recognize which sequences were modulators and which were not.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (scope of enablement) Applicants argue that the there is no suggestion that it would constitute undue experimentation to make or use any of the nucleotides within the scope of the claims (e.g., see pages 21-27 of the response). Applicants assert that various techniques are known in the art to create the sequences and determine if they meet the structural limitations of the claims; that routine experimentation is not undue; that the degree of unpredictability must be considered within the context of the invention and the knowledge of one of skill in the art; that not all compositions within the scope of the claims have the same efficacy or activity; that as long as the

specification discloses at least one method of making and using the invention the that bears a reasonable correlation to the to the entire scope of the claimed invention.

It is respectfully pointed out that the rejection was set forth in view of the written description rejection which clearly indicated the nature of the invention, the breadth of the claims, the amount of direction or guidance presented, the state of the prior art. It is noted that the claims are very broad and encompass all variants of SEQ ID NO: 1 that meet the structural limitations set forth in the claims, including variants which have completely different function as well as non-functional variants. The claims specifically encompass any nucleic acid that is greater than 91.6% identical to SEQ ID NO: 1. It is respectfully pointed out that SEQ ID NO: 1 is 887 nucleotides long. A nucleic acid that is 91.61% identical to SEQ ID NO:1 would be different at 74 different nucleotides wherein each of the 74 different nucleotides can be any one of three different nucleotides. Therefore, the claims encompass nucleic acids that have at least 1 and up to 74 different nucleotides wherein the nucleotide changes can be at any position within the sequence. In addition, the claims also encompass fragments or deletions of SEQ ID NO: 1 wherein the fragment or deletion variant meets the 91.6% identity limitation.

The number of possible polynucleotide sequences that are of a given percent identity relative to a reference sequence, where all differences between the possible sequences and the reference sequence are substitutions (note: the claims encompass substitutions as well as deletion variants) can be estimated by the following formula:

$$N = XL + X^2L(L-1)/2! + X^3L(L-1)(L-2)/3! + \ldots + X^{n-1}L(L-1)(L-2)\ldots(L-(n-2))/(n-1)! + X^nL(L-1)(L-2)\ldots(L-(n-1))/n!$$

(note: the first term gives the number of different sequences having one substitution, the second the number of sequences having two substitutions, and so on to the number with n substitutions).

where **N** is the number of different sequences, **X** is the number of different residues that can be substituted for a residue in the reference sequence, **L** is the length of the reference sequence, and **n** is the maximum number of residues that can be substituted relative to the reference sequence at a given % identity. For a nucleotide sequence, **X** is 3 (because there are 3 alternate nucleotides).

The last term of the formula can be simplified for estimating the number of different sequences to:

$X^n L!/n!(L-n)!$

In the instant case, a nucleotide sequence that is greater than 91.6 % identical to a polynucleotide sequence 887 nucleotides long (e.g., SEQ ID NO: 1) can have anywhere from 1 to 74 different nucleotide substitutions. Thus the claims encompass $3^{74}(887!)/74!(887-74)!$, which is more than $3x10^{100}$ different sequences. That is, the claims encompass more than 3,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000, 000,000,000,000,000,000,000,000,000,000,000,000 different sequences.

It is acknowledged that routine experimentation is not considered undue; however, making and testing all of these different sequences, including identifying the function of each one, is certainly an undue amount of experimentation considering that making and testing even 1,000,000 different sequences a day (a seemingly improbable task) would take an enormous amount of time to complete ($3x10^{100}/1,000,000= 3x10^{94}$ days, and $3x10^{94}$ days/365= $8x10^{91}$ years).

It is acknowledged that not every polynucleotide sequence would encode a different polypeptide. However, it is certainly possible that each of the 74 substitutions in the nucleotide sequence could result in a polynucleotide that encodes a different polypeptide. Since SEQ ID NO: 1 encodes a polypeptide that is 204 amino acids long (e.g., see SEQ ID NO: 2), the claims encompass polynucleotides encoding the 204 amino acid sequence of SEQ ID NO: 2 wherein the

sequences comprises 74 different amino acid substitutions wherein each substitution could be any one of 19 different amino acids. Therefore, it would still be an enormous task to make and identify the function of each of the polypeptides encoded by genus of polynucleotides encompassed by the claims.

Considering the huge breadth of claims in view of the lack of guidance provided in the specification with respect identification of any critical functional elements of the sequences, it would have required undue experimentation in order to make and use the full breadth of the claimed invention.

As such, Applicants arguments are not persuasive and the rejection is not withdrawn.

With respect to the rejection of claims under 35 USC 102(b) as being anticipated by KATO, Applicants assert that the claims have been amended to recite that there is greater than 91.6% identity between the claimed sequences and SEQ ID NO: 1. Applicants contend that since KATO only teaches a sequence that is 91.6% identical to SEQ ID NO:1, KATO does not anticipate the claims.

In response, it is respectfully pointed out that the claims encompass an isolated/recombinant nucleic acid sequences comprising a polynucleotide sequence having greater than 91.6% identity to SEQ ID NO: 1 wherein the sequence is distinct from SEQ ID NO: 37. The phrase "a polynucleotide sequence having greater than 91.6% identity to SEQ ID NO: 1" is interpreted as encompassing a polynucleotide sequence wherein any portion of the sequence is greater than 91.6% identical to any part of SEQ ID NO: 1. This interpretation consistent with the indication that the isolated nucleic acid is distinct from SEQ ID NO: 37 (130

nucleotides long) and consistent with the indication that the nucleic acid can be "from 15 base pairs to 2.5kB in length" (e.g., see claims 1 and 10).

As previously indicated, KATO teaches a nucleic acid sequence that is 91.6% identical to SEQ ID NO: 1. Specifically, KATO teaches a sequence having a sequence that is 99.9% identical to nucleotides 74-887 of SEQ ID NO: 1, and having sequence that is 100% identical to nucleotides 74-775 and 777-887 of SEQ ID NO: 1. Given the interpretation of the claims indicated above, KATO does teach a nucleic acid sequence having greater than 99.1% identical to any part of SEQ ID NO: 1. Therefore, KATO anticipates the instant claims and the rejection is proper.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Anne-Marie Falk

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